L9 ANSWER 9 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:263843 BIOSIS
DN PREV199799570446
TI Chelation and mobilization of cellular iron by different classes of chelators.
AU Zanninelli, G.; Glickstein, H.; Breuer, W.; Milgram, P.; Brissot, P.; Hider, R. C.; Konijn, A. M.; Libman, J.; Shanzer, A.; Cabantchik, Z. Ioav (1)
CS (1) Dep. Biological Chemistry, Inst. Life Sci., Hebrew Univ. Jerusalem, Jerusalem 91904 Israel
SO Molecular Pharmacology, (1997) Vol. 51, No. 5, pp. 842-852. ISSN: 0026-895X.
DT Article
LA English
AB **Iron chelators** belonging to three distinct chemical families were assessed in terms of their physicochemical properties and the kinetics of iron chelation in solution and in two biological systems. Several hydroxypyridinones, reversed siderophores, and desferrioxamine derivatives were selected to cover agents with different iron-binding stoichiometry and geometry and a wide range of lipophilicity, as determined by the octanol-water partition coefficients. The selection also included highly lipophilic chelators with potentially **cell**-cleavable ester groups that can serve as precursors of hydrophilic and membrane-impermeant **chelators**. **Iron** binding was determined by the chelator capacity for restoring the fluorescence of iron-quenched calcein (CA), a dynamic fluorescent metallosensor. The iron-scavenging properties of the chelators were assessed under three different conditions: (a) in solution, by mixing iron salts with free CA; lb) in resealed red **cell** ghosts, by encapsulation of CA followed by loading with iron; and (c) in human erythroleukemia K562 **cells**, by loading with the permeant CA-acetomethoxy ester, in situ formation of free CA, and binding of cytosolic labile iron. The time-dependent recovery of fluorescence in the presence of a given chelator provided a continuous measure for the capacity of the **chelator** to access the **iron**/CA-containing compartment. The resulting rate constants of fluorescence recovery indicated that chelation in solution was comparable for the members of each family of chelators, whereas chelation in either biological system was largely dictated by the lipophilicity of the free chelator. For example, desferrioxamine was among the fastest and most efficient iron scavengers in solution but was essentially ineffective in either biological system when used at ltoreq 200 mu-M over a 2-hr period at 37 degree . On the other hand, the highly lipophilic and potentially **cell**-cleavable hydroxypyridinones and reversed siderophores were highly efficient in all biological systems tested. It is implied that in K562 **cells**, hydrolysis of these chelators is relatively slower than their ingress and binding of intracellular **iron**. The **chelator**-mediated translocation of **iron** from **cells** to **medium** was assessed in 55Fe-**transferrin**-loaded K562 **cells**. The speed of iron mobilization by members of the three families of chelators correlated with the lipophilicity of the free ligand or the **iron-complexed chelator**. The acquired information is of relevance for the design of chelators with improved biological performance.

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AN 1984:273093 BIOSIS
DN BA78:9573
TI A LIPOPHILIC **IRON CHELATOR** CAN REPLACE **TRANSFERRIN** AS A STIMULATOR OF **CELL** PROLIFERATION AND DIFFERENTIATION.
AU LANDSCHULZ W; THESLEFF I; EKBLOM P
CS DEP. PATHOLOGY, UNIV. HELSINKI, HAARTMANINKATU 3, SF-00290 HELSINKI 29, FINL.
SO J CELL BIOL, (1984) 98 (2), 596-601.
CODEN: JCLBA3. ISSN: 0021-9525.
FS BA; OLD
LA English
AB Of the different growth supplements used in chemically defined **media**, only **transferrin** is required for differentiation of tubules in the embryonic mouse metanephros. Since **transferrin** is an Fe-carrying protein, the crucial role of Fe for tubulogenesis was determined. Differentiation of metanephric tubules in whole embryonic kidneys and in a transfilter system was studied. The tissues were grown in chemically defined **media** containing **transferrin**, apotransferrin, the metal-chelator complex ferric pyridoxal isonicotinoyl hydrazone (FePIH) and excesses of Fe3+. Although apotransferrin was not as effective as Fe-loaded **transferrin** in promoting proliferation in the differentiating kidneys, excess Fe3+ at up to 100 .mu.M, 5 times the normal serum concentration, could not promote differentiation or proliferation. Fe coupled to the nonphysiological, lipophilic **iron chelator**, pyridoxal isonicotinoyl hydrazone, to form FePIH, could sustain levels of **cell** proliferation and tubulogenesis similar to those attained by **transferrin**. The role of **transferrin** in **cell** proliferation during tubulogenesis is solely to provide Fe. Since FePIH apparently bypasses the receptor-mediated route of Fe intkae, the use of FePIH as a tool for investigating **cell** proliferation and its regulation is suggested.

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AN 1987:359060 BIOSIS

DN BA84:56463

TI REPLACEMENT OF **TRANSFERRIN** IN SERUM-FREE CULTURES OF MITOGEN STIMULATED MOUSE LYMPHOCYTES BY A LIPOPHILIC **IRON CHELATOR**.

AU BROCK J H; STEVENSON J

CS UNIV. DEP. BACTERIOLOGY AND IMMUNOLOGY, WESTERN INFIRMARY, GLASGOW G11 6NT, U.K.

SO IMMUNOL LETT, (1987) 15 (1), 23-26.
CODEN: IMLED6. ISSN: 0165-2478.

FS BA; OLD

LA English

AB Proliferation of mouse lymph node lymphocytes in response to concanavalin A in serum-free **medium** is normally dependent upon the presence of **transferrin**. In the absence of **transferrin**, little proliferation occurred, but the response was restored by addition of the **iron complex** of pyridoxal isonicotinoyl hydrazone (FePIH), a lipophilic **iron chelator**. Since cellular acquisition of PIH-bound iron is known not to involve the **transferrin** receptor, these results indicate that **transferrin** promotes lymphocyte proliferation solely because of its iron-donating properties, and does not provide any additional signaling event for proliferation.